



# Armed Forces College of Medicine

## AFCM



# Mycobacteria



# Intended Learning Objectives (ILOs)

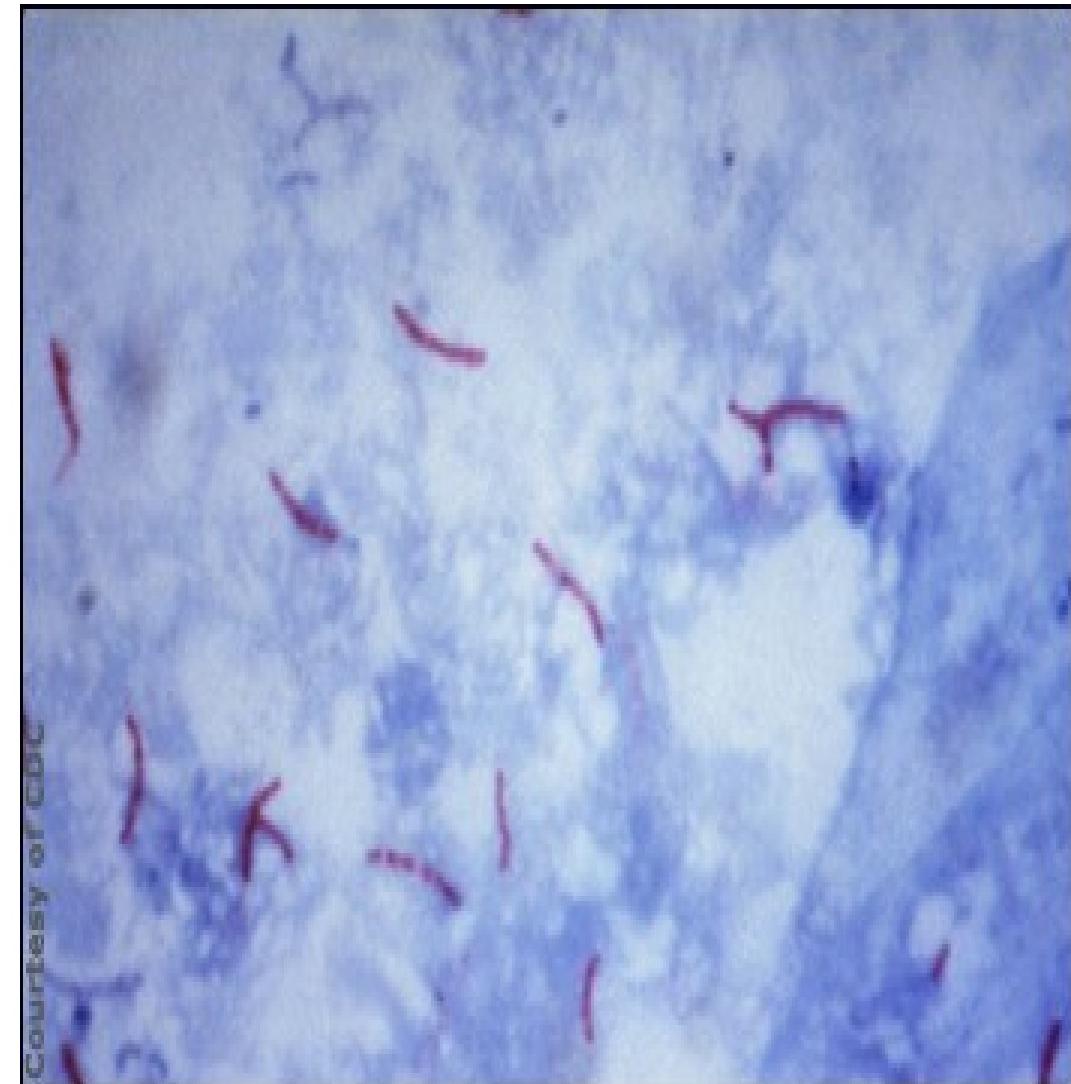
**By the end of this lecture the student will be able to:**

- **Describe pathogenesis & clinical manifestations of pulmonary TB**
- **Outline the laboratory diagnosis of pulmonary T.B.**
- **Outline prevention and control of pulmonary T.B.**



# Mycobacteria

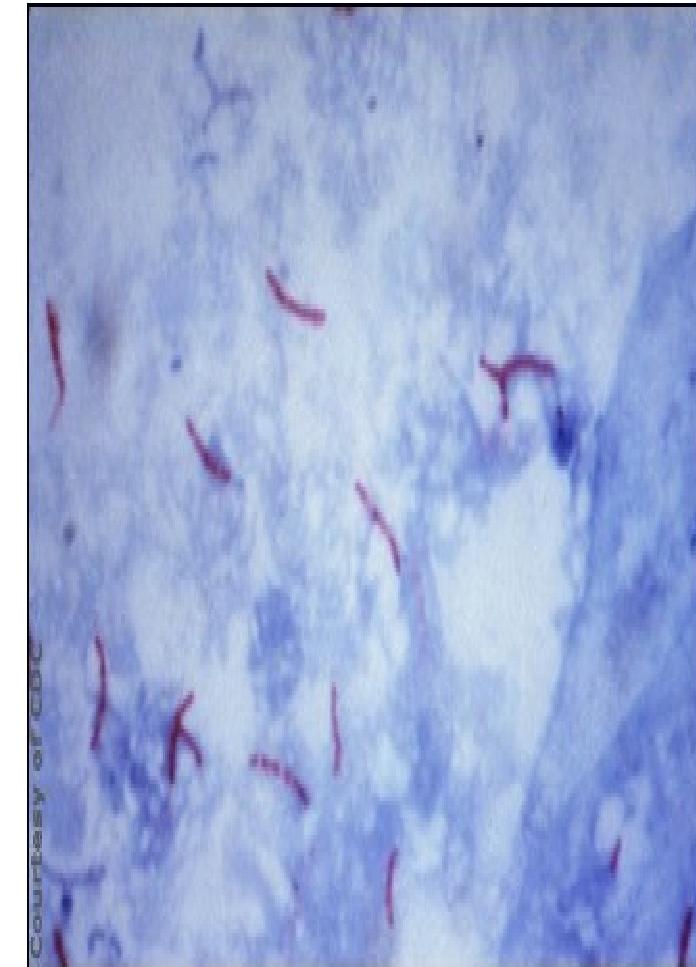
**Mycobacteria are aerobic bacilli that have an unusual cell wall, resulting in their inability to be Gram-stained.**





# Mycobacteria

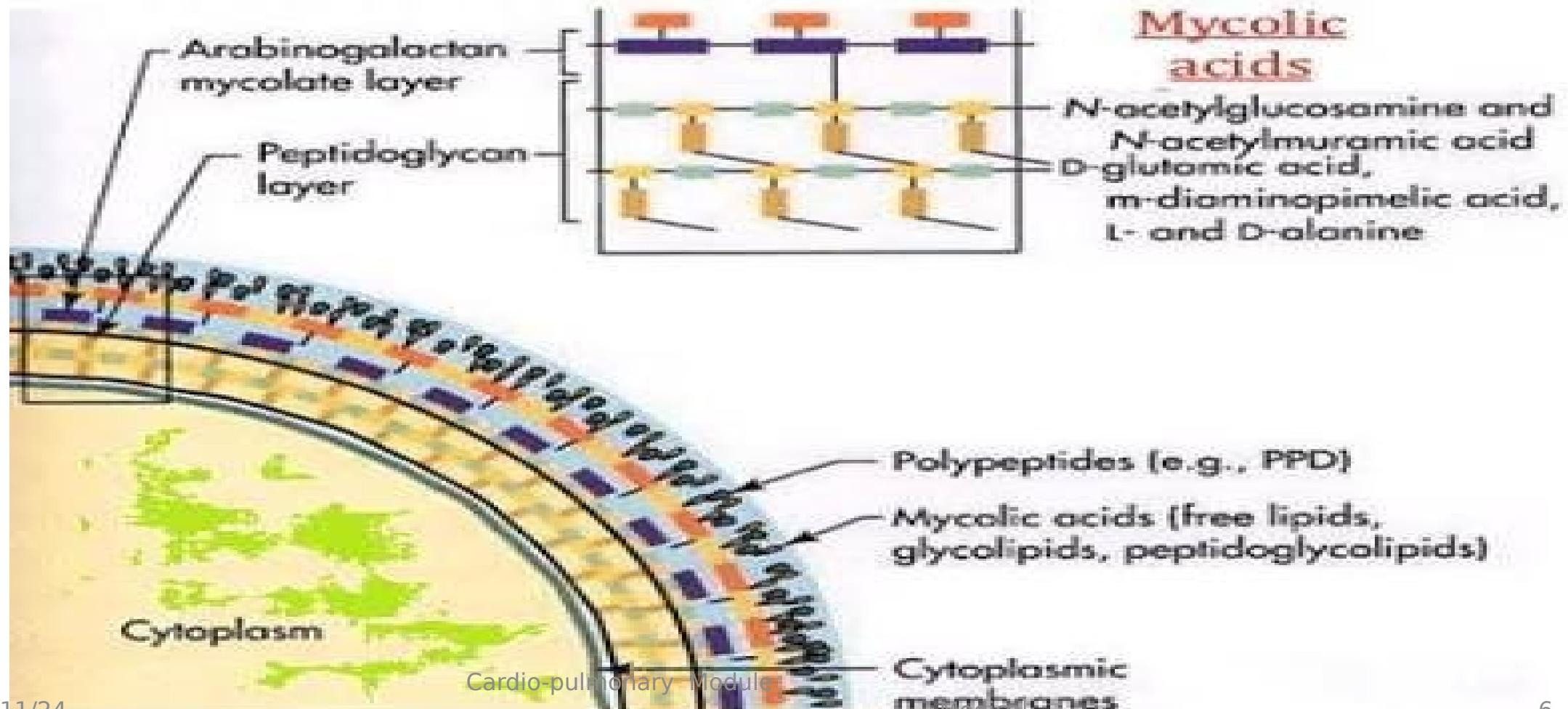
These bacteria are **ACID FAST** because they resist decolorization with acid/alcohol after being stained with carbol fuchsin. This is due to the high concentration of lipids, **mycolic acids**, in their cell wall



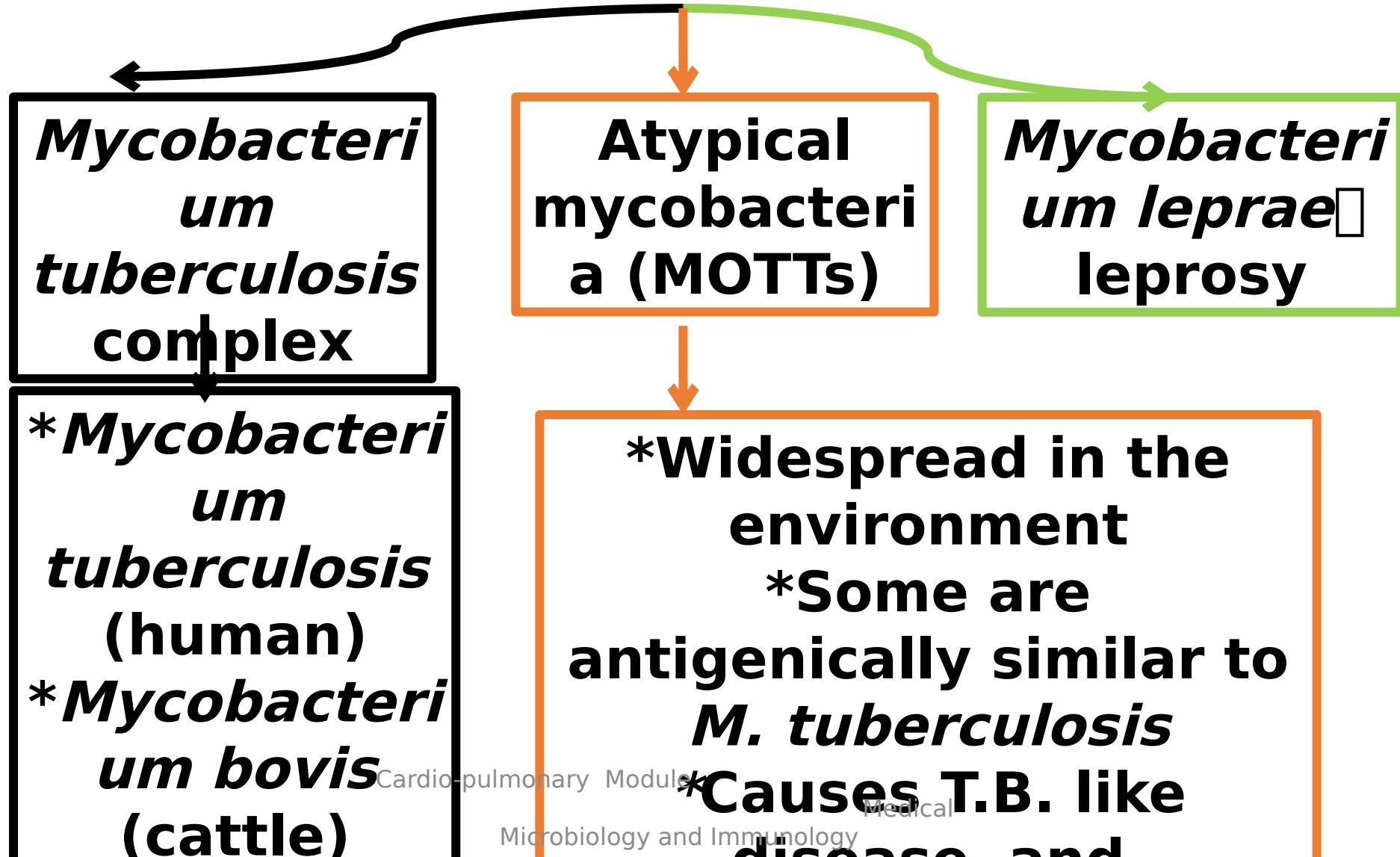
# Cell wall of Mycobacteria



## Lipid-Rich Cell Wall of Mycobacterium



# Members of Mycobacteria



# *Mycobacterium tuberculosis*- Disease



- This organism causes tuberculosis.
- Worldwide, *M. tuberculosis* causes more **deaths** than any other single microbial agent.
- One-third of the world's population is infected with this organism

# *Mycobacterium tuberculosis*- Properties



- *M. tuberculosis* is an **obligate aerobe** disease in highly oxygenated tissues (upper lobe of the lung and the kidney)
- Non motile non-capsulated and non-spore forming

# *Mycobacterium tuberculosis*- Properties



- Resistant to dehydration → survives in dried expectorated sputum

• **Grows slowly**



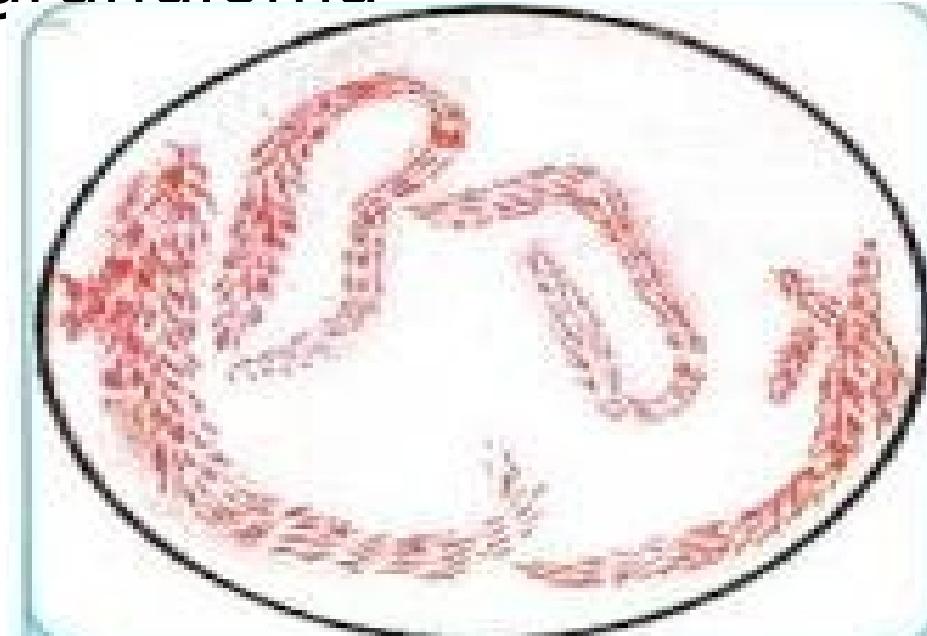
**Cultures incubated  
for 6 to 8 weeks  
before recording as  
negative**

**Prolonged  
course of  
TTT**



# *Mycobacterium tuberculosis*- Virulence factors

**1- Cord factor (glycolipid):** Virulent strains grow in a characteristic “serpentine” cordlike pattern, as the bacilli stick together → toxic to leukocytes + antichemotactic + development of granuloma



Cardio-pulmonary Module

9/11/24



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# *Mycobacterium tuberculosis*- Virulence factors

**2- Several antigenic proteins** elicit hypersensitivity reactions

**3- Mycolic acid:** inhibits formation of phagolysosome in macrophage→ *INTRACELLULAR SURVIVAL.*

**4- Metabolically inactive:** difficult to kill by antibiotics

**5- Antibiotic resistance:** acquired by chromosomal gene mutation.



# *Mycobacterium tuberculosis*- Transmission

## ***Mycobacterium tuberculosis***

- Person to person by respiratory AEROSOLS (mostly from smear positive patients) □ Lung □ reside in MQ.
- Humans are natural reservoir

## ***Mycobacterium bovis***

- Ingestion of unpasteurized milk from infected cows □ intestinal tuberculosis

Risk factors: Immune suppression, poor housing, poor nutrition



# Pathogenesi

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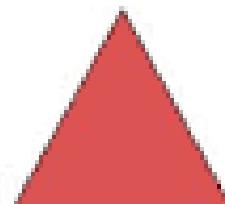
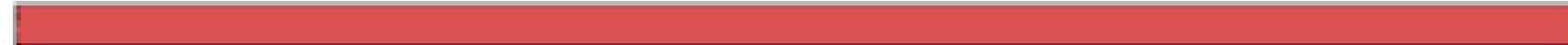
- **NO** exotoxin... **NO** endotoxin
- MQ infection[] phagosome[] mycolic acid inhibits its fusion with lysosomes[] the organism escapes the degrading lysosomal enzymes[] Intracellular survival.



Infection



Immunity

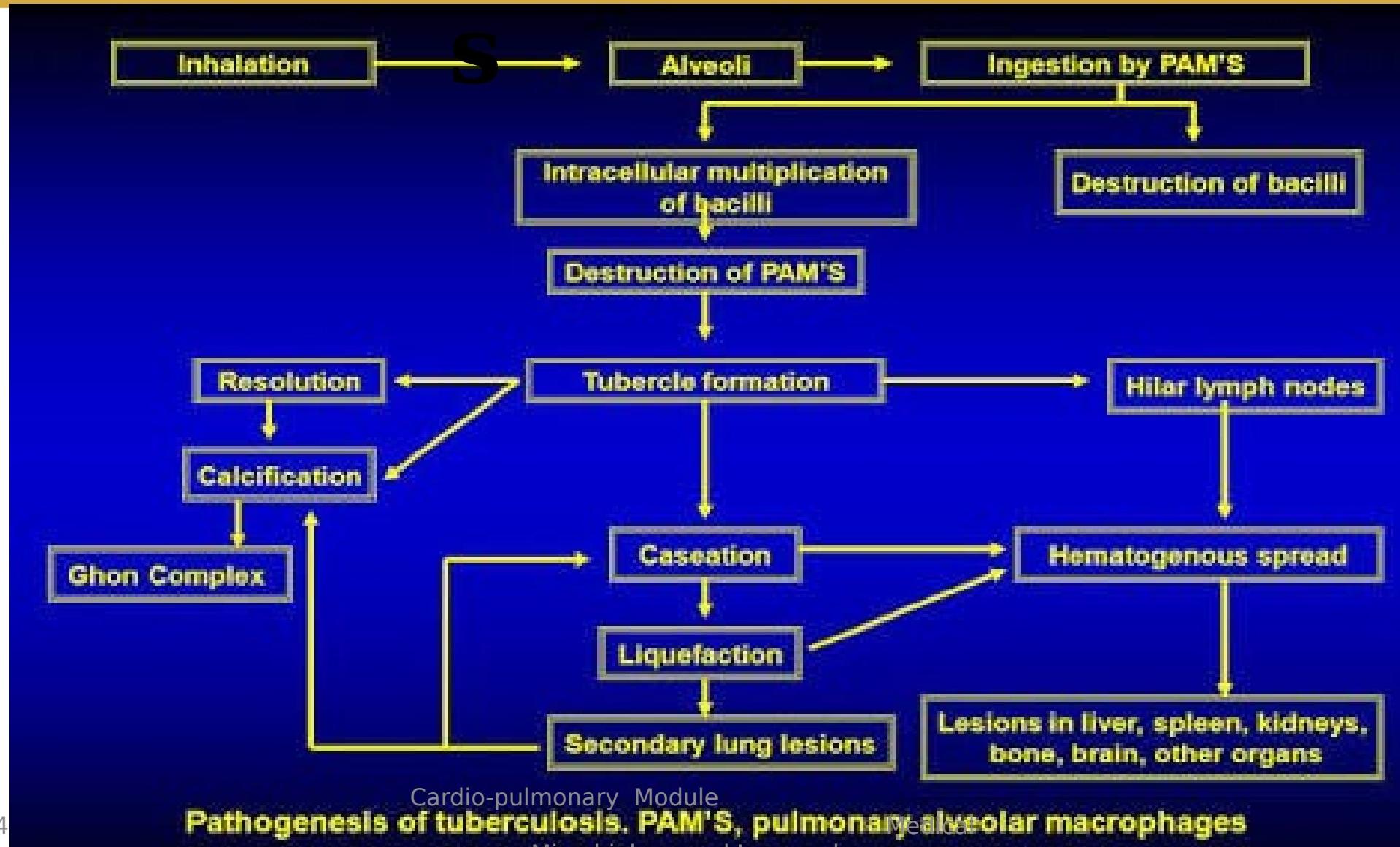


Cardio-pulmonary Module

Microbiology and Immunology

Medical

# Pathogenesis





# Pathogenesi

Spread of the organism within the body occurs by two ways:

**Tubercle erodes into a bronchus, empties its caseous contents** → **spread of the organism to other parts of the lungs, to the GIT if swallowed, and to other persons if expectorated**

→ **Via the bloodstream to many internal organs if cell-mediated immunity fails to contain the initial infection or at a late stage if a person becomes immunocompromised**

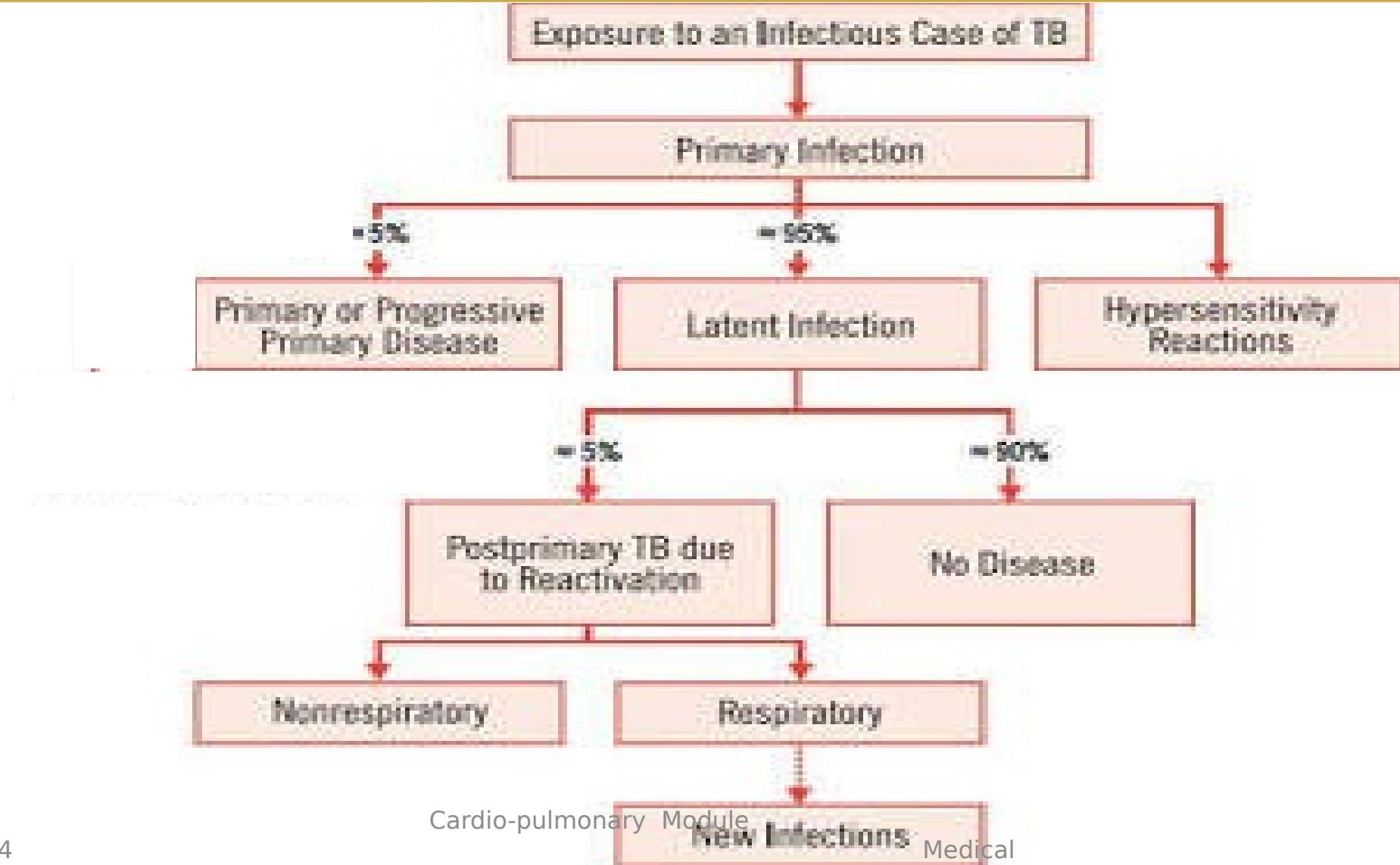
# Immunity and Hypersensitivity



- After recovery from the primary infection, resistance to the organism is mediated by **Th-1**
- Circulating antibodies also form. Do they have a role in resistance??



# Clinical findings



# Clinical findings



- **Asymptomatic: Latent infection...**
- **Generally: fever, night sweating, weight loss**
- **Pulmonary: cough, expectoration..  
Hemoptysis??**
- **Extrapulmonary: lymphadenitis (most common), erythema nodosum**



# Clinical findings

- **GIT:** abdominal pain and diarrhea, intestinal obstruction or hemorrhage may occur.
- **Oropharyngeal tuberculosis:** painless ulcer + lymphadenopathy

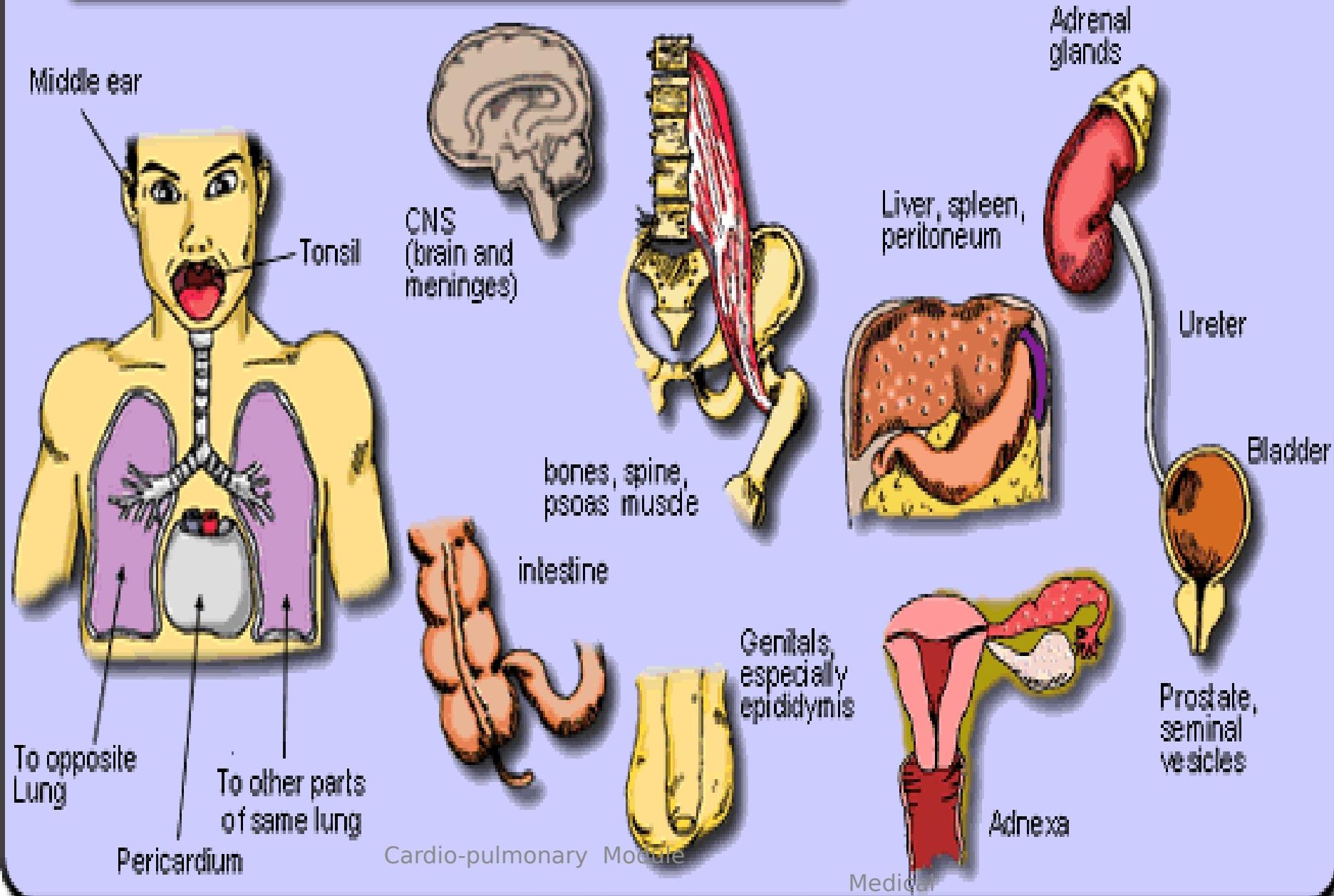


# Clinical findings

- **Renal tuberculosis:** mostly reactivation lesion□ dysuria, hematuria, and flank pain occur. “**Sterile pyuria**” is a characteristic finding????
  - **Miliary T.B.:** multiple disseminated lesions resembling millet seeds
- **Tuberculous meningitis** and **tuberculous osteomyelitis**, specially vertebral osteomyelitis (Pott's disease), are important disseminated forms.



# Tuberculosis Affects Many Parts of the Body





# Laboratory Diagnosis

1- **Acid fast staining** of sputum or other specimens by **ZN** stain

2- **Isolation and identification:** culture is performed on **L.J.** medium[] incubated for up to **8 weeks**

- In liquid BACTEC medium, radioactive metabolites are present, and growth can be detected by the production of radioactive carbon dioxide in about **2 weeks.**

**OBSOLETE**

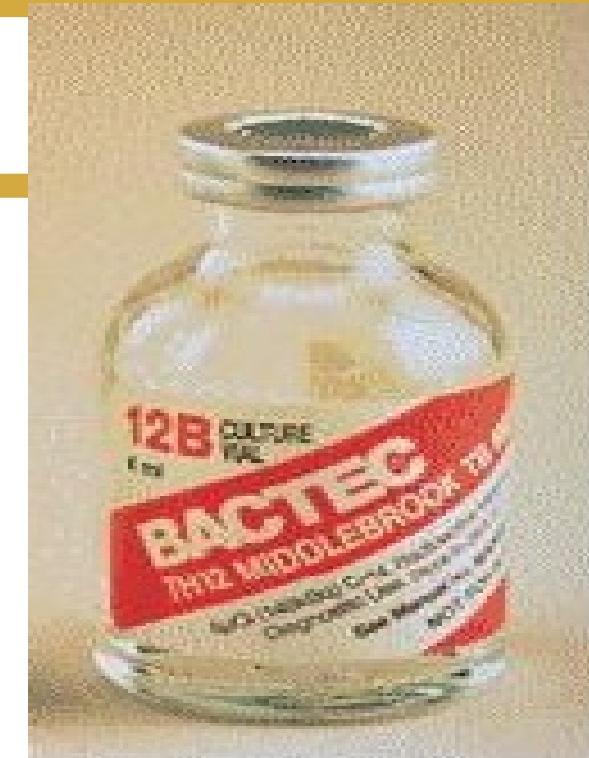
3- **PCR and nucleic acid amplification techniques:** detect the presence of *M. tuberculosis* directly in clinical specimens





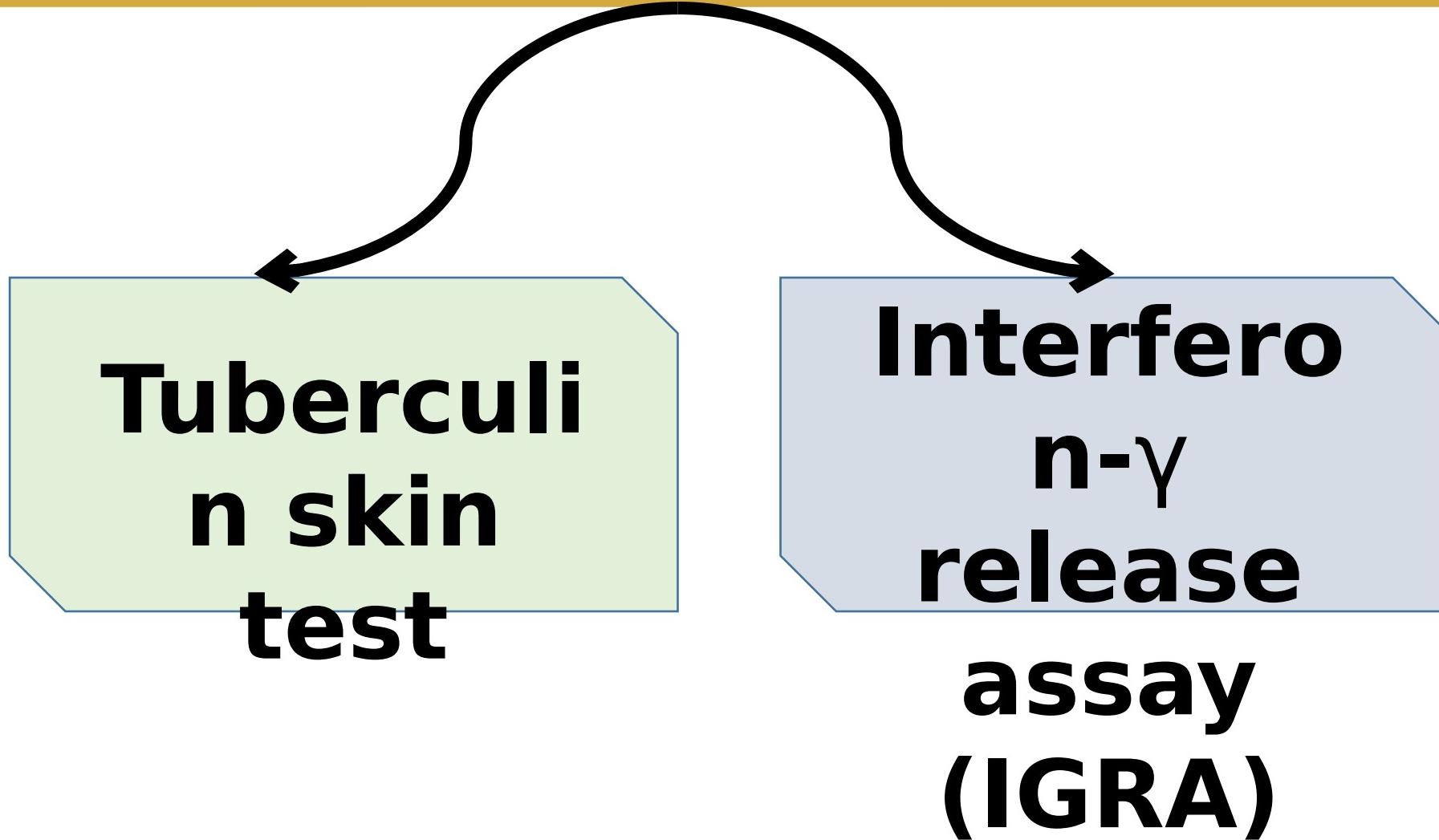
Specimen containing TB

Utilize  $^{14}\text{C}$  labeled palmitic as  
a single carbon source



Radioactive  
 $\text{CO}_2$

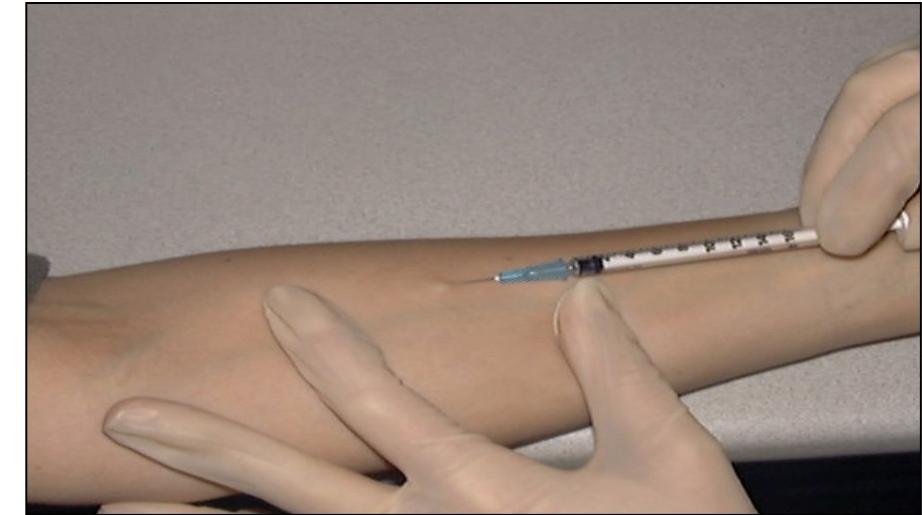
# Laboratory Diagnosis of Latent TB.





# Tuberculin skin test

Purified protein derivative (**PPD**) is the antigen used intra-dermally to induce hypersensitivity within 72 hours. Induration surrounding the test site is measured, its diameter depending on the status of the individual being tested.





# Tuberculin skin test

- The test is considered **positive** when the diameter is:

**15 mm or more**

- In a person who has no known risk factors

**10 mm or more**

- In a person with high-risk factors, (homeless person, intravenous drug users, medical staff).

**5 mm or more**

- In a person who has deficient cell-mediated immunity (e.g. AIDS patients) or close contact with a person with active tuberculosis



# Tuberculin skin test

- **A positive skin test result indicates previous exposure to the organism but not necessarily active disease.**
- The tuberculin test becomes positive 4 to 6 weeks after infection

# Interferon- $\gamma$ release assay (IGRA)

Blood cells from the patient are exposed to antigens from *M. tuberculosis* (in vitro test)

\*\*This antigen is NOT PRESENT in BCG



Amount of interferon- $\gamma$  released from the cells is measured

## Advantages??

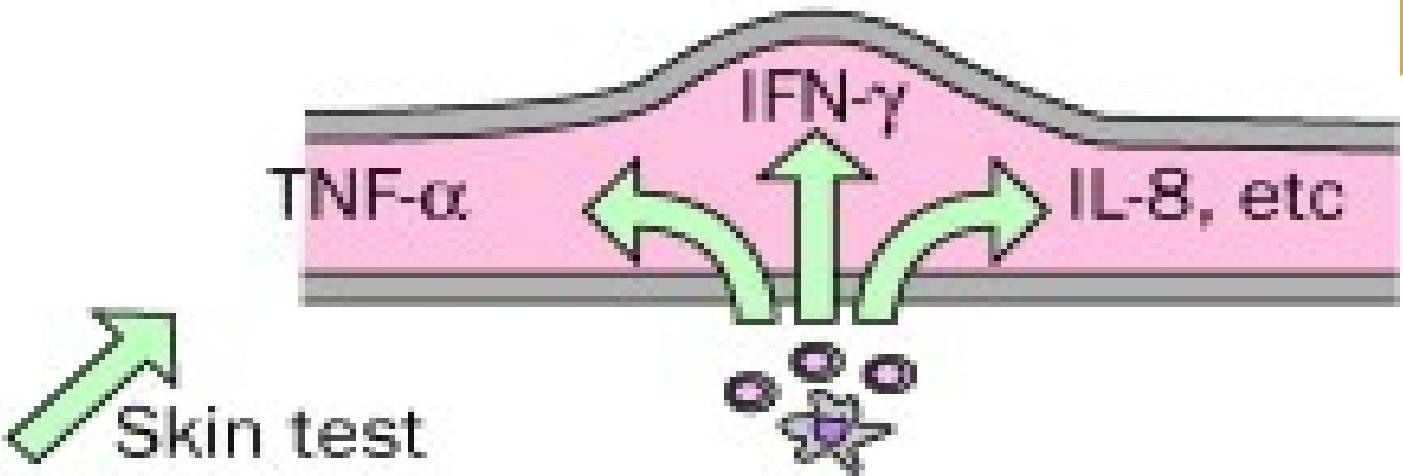
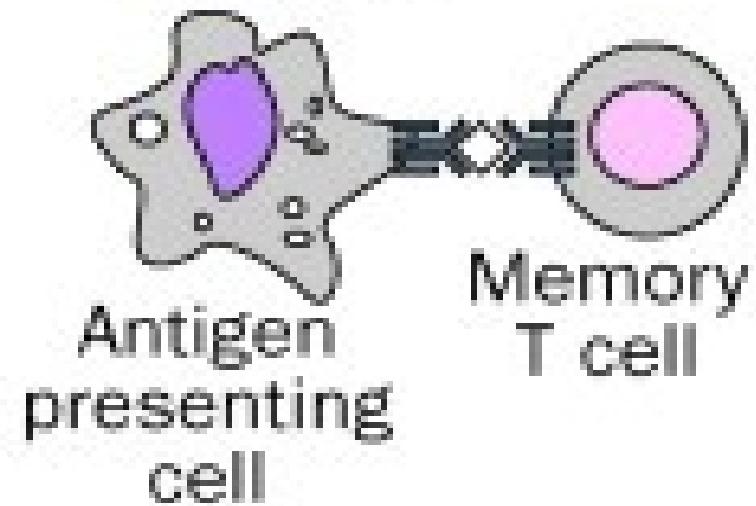
Cardio-pulmonary Module

Medical

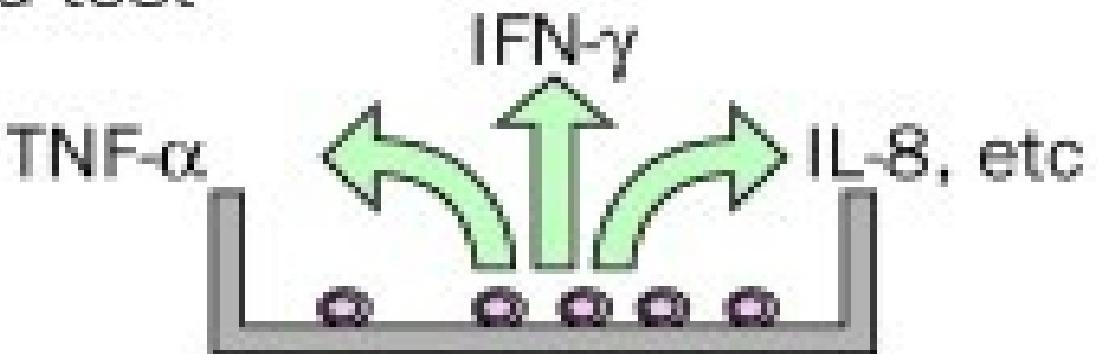
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## Measurement of induration and erythema

### Presentation of mycobacterial antigens



in-vitro  
blood test



### Measurement of IFN- $\gamma$ production

# Emergence of T.B.



- **Tuberculosis emerging today as a leading infectious killer of youth and adult all over the world:**

- 1- Increased incidence of HIV infection.
- 2-Emergence of MDR strains.
- 3- \_\_\_\_\_



# Prevention of T.B.



**1- BCG vaccine:** induces partial resistance to tuberculosis. **Does not** prevent disease. Prevents mortality in children under 5 years of age.

The vaccine contains a strain of **live-attenuated** *M. bovis* called **Bacillus Calmette-Guérin**.

- Effectiveness ranges from 0% to 70%.



- 2- Pasteurization of milk prevents intestinal T.B.**
- 3- To prevent spread to medical personnel, other patients and the environment: Airborne isolation precautions**
- 4- Tuberculin skin test to detect recent converters in: people with HIV infection, close contacts of patients with active tuberculosis, alcoholics and intravenous drug users, HCWs exposed to patients**